UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/633,629	08/05/2003	Ayoub Rashtchian	60126-002US	6375

61263 7590 06/05/2009

PROSKAUER ROSE LLP
1001 PENNSYLVANIA AVE, N.W.,
SUITE 400 SOUTH
WASHINGTON, DC 20004

EXAMINER	
POPA, ILEANA	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
06/05/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/633,629	RASHTCHIAN ET AL.	
	Examiner	Art Unit	
	ILEANA POPA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/19/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-24 have been cancelled. Claims 25-42 are new. The new claims 25-42 are directed to the invention the originally claimed.

Claims 25-42 are pending and under examination.

2. All rejections pertaining to claims 1-4, 7-18, and 21-23 are moot because Applicant cancelled the claims in the reply filed on 03/04/2009.

New Rejections

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 25-27, 32-36, 38, and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al. (Brain Research Protocols, 2000, 5: 211-217, of record), in view of both Lopez Garcia et al. (Analyst, 1991, 116: 517-520) and Stemmer et al. (US Patent No. 5,834,252, of record).

Li et al. teach quantification of mRNA expression by TaqMan hot-start real-time RT-PCR, wherein the real-time RT-PCR is carried out in a MicroAmp Optical 96-well reaction plate to detect multiple target nucleic acids, wherein each well contains an

aliquot of a master mix comprising Tween 20 and AmpliTaq Gold DNA polymerase (i.e., a thermostable polymerase), and wherein the amplified mRNA is optically detected (claims 25-27, 32-36, 38, and 42) (Abstract; p. 212, column 1, Supply and reagents; p. 213, column 1 bridging column 2 and Fig. 1).

Li et al. do not teach including and anti-foam agent in their master mix (claims 25 and 38). However, doing such is suggested by the prior art. For example, Lopez Garcia et al. teach that the small air bubbles formed in the presence of detergents worsen the reproducibility of quantification by optical detection; Lopez Garcia et al. teach using anti-foam agents to overcome this problem (p. 518, column 1). Stemmer et al. teach that anti-foam agents could be used in PCR (i.e., the anti-foam agents do not substantially inhibit the polymerase) (column 10, lines 7-30). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Li et al. by further including an anti-foam agent in their master mix to achieve the predictable result of improving the reproducibility (i.e., accuracy) of optical detection in RT-PCR. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

5. Claims 25-28, 32-38, and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al. taken with both Lopez Garcia et al. and Stemmer et al., in further view of Blaschke et al. (J Immunol Methods, 2000, 246: 79-90, of record).

The teachings of Li et al., Lopez Garcia et al., and Stemmer et al. are applied as above for claims 25-27, 32-36, 38, and 42. Li et al., Lopez Garcia et al., and Stemmer

et al. teach using TaqMan probes and not a fluorescent nucleic acid-binding dye (claims 28 and 37). Blaschke et al. teach that real-time RT-PCR can be performed by using either TaqMan probes or nucleic acid-binding dyes (p. 80, column 2, first paragraph, p. 82, column 1, second paragraph). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Li et al., Lopez Garcia et al., and Stemmer et al. by replacing their TaqMan probe with a nucleic acid-binding dye to achieve the predictable result of quantifying the RT-PCR products. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

6. Claims 25-27, 29-36, and 38-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al. taken with both Lopez Garcia et al. and Stemmer et al., in further view of each Kyle (US Patent No. 5,658,767, of record), Sigma catalog (1998, of record) and Wierenga (US Patent No. 5,968,889, of record).

The teachings of Li et al., Lopez Garcia et al., and Stemmer et al. are applied as above for claims 25-27, 32-36, 38, and 42. Li et al., Lopez Garcia et al., and Stemmer et al. do not specifically teach using 520-US as an anti-foam agent (claims 30 and 40). Kyle et al. teach the 1520-US as a suitable silicone-based anti-foaming agent (column 11, Example 3). It would have been obvious to one of skill in the art, at the time the invention was made, to use the method of Stemmer et al. with 1520-US as an anti-foam agent to achieve the predictable result of improving the reproducibility (i.e., accuracy) of optical detection in RT-PCR.

Li et al., Lopez Garcia et al., Stemmer et al., and Kyle do not teach using two anti-foam agents (claims 29, 31, 39, and 41). However, doing such is suggested by the prior art. For example, the Sigma catalog teaches that anti-foaming agents can be supplied as a mixture of organic anti-foams and silicone-based anti-foams, and that O-30 is an organic antifoaming agent. Wierenga teaches that silicone-based anti-foaming agents are not that effective, and that the addition of organic anti-foamers results in a synergistic anti-foaming combination (Abstract, column 1, lines 38-51, and also column bridging column 2). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Li et al., Lopez Garcia et al., Stemmer et al., and Kyle by further adding an organic anti-foamer such as O-30, with a reasonable expectation of success. The motivation to do so is provided by Wierenga who teaches that the addition of organic anti-foamers to silicone-based anti-foamers results in a synergistic anti-foaming combination. One of skill in the art would have had a reasonable expectation of success in using such a combination because Sigma catalog describes such combinations and because the art teaches that such combinations are very efficient in controlling foam formation. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

Applicant's arguments are answered below to the extent that they apply to the instant rejections.

Applicant's arguments regarding Stemmer et al. were previously presented. Applicant also argues surprising results. Specifically, Applicant argues, the specification

shows that the instantly claimed method surprisingly allows detection measurements that are free of artifacts. For example, FIGS 2 and 4 of the instant specification illustrate the deleterious effect of foaming on threshold cycle (Ct) determination in real-time PCR from identical reactions containing 20 copies of template DNA per reaction. The only difference between the two reactions is the inclusion of antifoam in the reactions recorded in FIG 4. FIG 2 shows that fluorescence readings were distorted with respect to baseline and Ct determinations in qPCR reactions without the addition of anti-foaming agents. Specifically the bubble error in wells H1 to H6 resulted in Ct values ranging from 33 to 38, which represents approximately a 15 fold difference. FIG 4, however, surprisingly shows that the addition of anti-foam not only limited bubble formation, but produced a stable baseline allowing for a more accurate reading. The greatest variation in these antifoam containing tests was 1 Ct, which represent approximately a 2 fold difference in quantification. Therefore, Applicant requests the withdrawal of the rejection.

Applicant's arguments are acknowledged, however, the rejection is maintained for the following reasons:

The arguments related to Stemmer et al. were previously addressed. The argument of surprising results is not found persuasive because the prior art teaches that the use of anti-foam agents improve the accuracy of optical detection of samples comprising detergents (see the rejection above).

7. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ileana Popa/
Primary Examiner, Art Unit 1633